

### **REMARKS**

Upon entry of the present Amendment, claims 1-22 and 24-47 will be pending. Claims 48-54 are cancelled as non-elected claims. Claim 23 is cancelled and the limitation in this claim is incorporated into amended claim 1. Applicants reserve the rights to pursue the canceled subject matter in a subsequent application. The above-described amendments do not introduce any new matter into the present application.

#### **Restriction requirement**

Applicants appreciate the Examiner's acknowledgement of Applicants' election without traverse of Group I, claims 1-47. Claims 48-54 are cancelled as non-elected claims.

#### **Information Disclosure Statement**

Applicants appreciate the Examiner's review and consideration of the references listed on the 1449 received 11 July 2002 in Paper No.8 and the International Search Report submitted with Paper No. 8. Applicants, however, noticed that references 10-12 submitted with the July 1, 2002 Information Disclosure Statement (Paper No.8) have not been considered, presumably due to the fact that these references are not in English. Applicants enclose herein an English abstract for each of the references (Exhibits A-C). Applicants respectfully request the Examiner to consider the references, in light of the newly submitted English abstracts, and make the references of record in the present application.

#### **Rejections under 35 U.S.C. § 112**

Claims 3, 9, 21, 22, 25 and 34-38 are rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

These rejections have been overcome by the amendments of claims 3, 9, 21, 22 and 34-38 as suggested by the Examiner.

It is respectfully submitted that the rejection of claims 3, 9, 21, 22, 25 and 34-38 under 35 U.S.C. § 112 is overcome by the above remarks and/or amendments and must be withdrawn.

#### **Rejection under 35 U.S.C. § 102**

##### **Rava**

Claims 1-18, 26-33, 36, 38-41, 46 and 47 are rejected under 35 U.S.C. 102(b) as being allegedly anticipated by Rava et. al., U.S. Patent No. 5,545,531 (Rava). Regarding Claim 1, Rava is alleged to disclose an integrated device comprising a substrate comprising a plurality of distinct micro-locations and a plurality of microchips wherein the number of micro-locations equals the number of said microarrays chips (Column 8, lines 1-27 and Fig. 4-6).

This rejection has been overcome by the amendment of claim 1. Claim 1, in its presently amended form, recites "the microlocation(s) is thermally insulated by an inert gas," which is not disclosed in Rava. Claims 2-22 and 24-47 are not anticipated by Rava as these claims depend on claim 1.

##### **Zhou**

Claims 1-6, 8, 10, 13-22, 26-27, 31-33, 36, 38-41, 46 and 47 are rejected under 35 U.S.C. 102(e) as being allegedly anticipated by Zhou et. al., U.S. Patent No. 6,355,491 B1 (Zhou). Regarding Claim 1, Zhou is alleged to disclose an integrated device comprising a substrate comprising a plurality of distinct micro-locations and a plurality of microchips wherein the number of micro-locations equals the number of said microarrays chips (Column 6, line 53 - Column 7, line 24).

This rejection is respectfully traversed. As disclosed at column 6, line 53 through column 7, line 24, a portion of Zhou cited by the Examiner, Zhou discloses a single biochip, not an integrated microarray device comprising a substrate comprising a plurality of distinct microlocations and a plurality of microarray chips. In any case, this rejection has been overcome by the amendment of claim 1. Claim 1, in its presently amended form, recites "the

microlocation(s) is thermally insulated by an inert gas," which is not disclosed in Zhou. Claims 2-22 and 24-47 are not anticipated by Zhou as these claims depend on claim 1.

It is respectfully submitted that the rejection of claims 1-22, 26-33, 36, 38-41, 46 and 47 under 35 U.S.C. § 102 is overcome by the above remarks and/or amendments and must be withdrawn.

**Rejection under 35 U.S.C. § 103**

**Rava in view of Yasuda**

Claims 19-22, 34, 35, 37 and 42-45 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Rava in view of Yasuda et. al., U.S. Patent No. 6,093,370 (Yasuda).

This rejection is respectfully traversed. Rava and Yasuda, whether alone or in combination, do not render the presently claimed invention obvious because there is no motivation, whether explicitly or implicitly, to combine the teachings of Rava and Yasuda to arrive at the presently claimed integrated microarray devices.

The nature of the motivation required in order to justify combining documents in support of an art rejection has been outlined by the Federal Circuit in *In re Rouffet*, 47 USPQ2d 1453 (Fed. Cir. 1998). As there clearly set forth, only three recognized motivations are acceptable. The first is a suggestion in the documents themselves. There is no such suggestion here either in Rava or Yasuda to combine the teachings of the two references. The second possible rationale lies in the nature of the problem to be solved. What problem would this be? Rava teaches methods for concurrently processing multiple biological chip assays by providing a biological chip plate comprising a plurality of test wells, each test well having a biological chip having a molecular probe array (See abstract and Figures 4-6). Yasuda teaches a process and apparatus for selectively extracting a trace quantity of a target polynucleotide (DNA or RNA) by modifying each of independent split areas on the surface of a substrate separately with each of probes (specific oligonucleotides) having different base sequences respectively, hybridizing polynucleotides (DNA or RNA) in the sample solution separately to the probes, and then heating

a specific area alone of the substrate selectively to allow a polynucleotide alone complementarily hybridized with the heated probe to liberate from the probe (See column 2, lines 21-30 and various figures of Yasuda). Thus Rava and Yasuda use two totally different operational principles and there is no common problem to be solved here. The third and final criterion is clearly not present - the notorious nature of at least one document cited such that everyone in the field would be expected to be aware of it.

In addition, even assuming, *arguendo*, there were motivation to combine the references, combination of the teachings of these references would not result in all the elements of presently pending claims. Each of the presently pending claims has the limitation "the microlocation(s) is thermally insulated by an inert gas." As recognized by the Examiner, neither Rava nor Yasuda teaches or suggests such a limitation.

Rava in view of Yasuda and further in view of Schembri

Claims 23-25 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Rava as applied to claim 19 above and further in view of Schembri et. al., U.S. Patent No. 6,258,593 (Schembri).

Regarding claims 23-25, the Examiner acknowledges that Rava and Yasuda do not specifically teach that the microlocations are thermally insulated by an inert gas (claim 23) wherein the inert gas is air (claim 24) and wherein the insulated air is contained between the walls of adjacent wells. The Examiner, however, alleges that Schembri teaches a similar device wherein the microlocations are thermally insulated by air between the walls of adjacent wells (Fig. 1-3). The Examiner asserts that it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the insulation of Schembri to the space between the wells of Rava and Yasuda to thereby insulate the wells from each other for the obvious benefits of maintaining environmental control of each individual microlocation. The Examiner further asserts that one skilled in the art would have been motivated to thermally

insulate the microlocations to thereby optimize thermal conditions for each microlocation based on the test being performed thereon.

This rejection is respectfully traversed. Rava, Yasuda and Schembri, whether alone or in combination, do not render the presently claimed invention obvious because there is no motivation, whether explicitly or implicitly, to combine the teachings of Rava, Yasuda and Schembri to arrive at the presently claimed integrated microarray devices.

In fact, Schembri teaches away from such combination to arrive at the presently claimed invention. The test for "teaching away" is that a "reference will teach away if it suggests that the line of development flowing from the reference's disclosure is unlikely to be productive of the result sought by the applicant." *In re Gurley*, 27 F.3d 551, 553, 31 USPQ.2D 1130, 1131 (Fed. Cir. 1994). In addition, if proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984) (Claimed device was a blood filter assembly for use during medical procedures wherein both the inlet and outlet for the blood were located at the bottom end of the filter assembly, and wherein a gas vent was present at the top of the filter assembly. The prior art reference taught a liquid strainer for removing dirt and water from gasoline and other light oils wherein the inlet and outlet were at the top of the device, and wherein a pet-cock (stopcock) was located at the bottom of the device for periodically removing the collected dirt and water. The reference further taught that the separation is assisted by gravity. The Board concluded the claims were *prima facie* obvious, reasoning that it would have been obvious to turn the reference device upside down. The Court reversed, finding that if the prior art device was turned upside down it would be inoperable for its intended purpose because the gasoline to be filtered would be trapped at the top, the water and heavier oils sought to be separated would flow out of the outlet instead of the purified gasoline, and the screen would become clogged.).

The Examiner's allegation that that Schembri teaches a device wherein the microlocations are thermally insulated by air between the walls of adjacent wells is erroneous.

First, the chamber of the devices taught in Schembri are sealed by mechanical means and not by air (See e.g., Figures 1-3 and column 10, line 57 through column 11, line 52 of Schembri). The only use of air bubble taught in Schembri is to facilitate mixing of contents of the enclosed chamber (See, column 5, lines 19-20, lines 47-56, column 10, lines 8-14, lines 48-53, column 12, lines 1-2, lines 25-42, lines 54-58, column 17, lines 4-6, lines 16-20 and in claim 12). On the other hand, if Schembri were to be combined with Rava and Yasuda, as suggested by the Examiner, to arrive at the presently claimed integrated microarray devices, the air would be located between microlocations and not in any microlocations. This modification would make the intended use of air, i.e., facilitating mixing of contents of the enclosed chamber, as taught in Schembri, impossible. And this is impermissible under the well established legal precedents.

It is respectfully submitted that the rejections of claims 19-25, 34, 35, 37 and 42-45 under 35 U.S.C. § 103 have been overcome by the above remarks and/or amendments and must be withdrawn.

#### **Double patenting**

##### **Zhou**

Claims 1-8, 10, 13-22, 26-27, 31-33, 36, 38-41, 46 and 47 are rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-40 of Zhou.

This rejection is respectfully traversed. As discussed above in connection with the anticipation rejection, claims 1-40 of Zhou are directed to a single biochip, not an integrated microarray device comprising a substrate comprising a plurality of distinct microlocations and a plurality of microarray chips. In addition, as recognized by the Examiner, Zhou does not disclose, let alone claim, a device wherein the microlocations are thermally insulated, not to mention thermally insulated by an inert gas.

##### **Cheng**

Claims 1-47 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-139 of Cheng et al., U.S. Patent No. 6,403,367 (Cheng).

This rejection is respectfully traversed. None of claims 1-139 of Cheng is directed to an integrated microarray device comprising a substrate comprising a plurality of distinct microlocations and a plurality of microarray chips and wherein the microlocations are thermally insulated by an inert gas.

It is respectfully submitted that the rejections of claims 1-47 under the judicially created doctrine of obviousness-type double patenting have been overcome by the above remarks and/or amendments and must be withdrawn.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 514572000100.

Respectfully submitted,

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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

**In the Claims:**

1. (Amended) An integrated microarray device, which device comprises a substrate comprising a plurality of distinct microlocations and a plurality of microarray chips, wherein the number of said microlocations equals to or is more than the number of said microarray chips, and wherein the microlocation(s) is thermally insulated by an inert gas.
3. (Amended) The device of claim 2, wherein the substrate comprises a silicon and the silicon is silicon dioxide or silicon nitride.
9. (Amended) The device of claim 1, wherein the number microlocations and the distance [among the] between each microlocations [correspond] are the same as to a standard microtiter plate.
21. (Amended) The device of claim 10, wherein the microlocations are wells and at least one of the wells is thermally insulated.
22. (Amended) The device of claim 10, wherein the microlocations are wells and all of the wells are thermally insulated.
34. (Amended) The device of claim 33, wherein the moiety is a cell and the cell is selected from the group consisting of an animal cell, a plant cell, a fungus cell, a bacterium cell, a recombinant cell and a cultured cell.



35. (Amended) The device of claim 33, wherein the moiety is a cellular organelle and the cellular organelle is selected from the group consisting of a nuclei, a mitochondrion, a chloroplast, a ribosome, an ER, a Golgi apparatus, a lysosome, a proteasome, a secretory vesicle, a vacuole and a microsome.

36. (Amended) The device of claim 33, wherein the moiety is a molecule and the molecule is selected from the group consisting of an inorganic molecule, an organic molecule and a complex thereof.

37. (Amended) The device of claim 36, wherein the moiety is an inorganic molecule and the inorganic molecule is an ion selected from the group consisting of a sodium, a potassium, a magnesium, a calcium, a chlorine, an iron, a copper, a zinc, a manganese, a cobalt, an iodine, a molybdenum, a vanadium, a nickel, a chromium, a fluorine, a silicon, a tin, a boron and an arsenic ion.

38. (Amended) The device of claim 36, wherein the moiety is an organic molecule and the organic molecule is selected from the group consisting of an amino acid, a peptide, a protein, a nucleoside, a nucleotide, an oligonucleotide, a nucleic acid, a vitamin, a monosaccharide, an oligosaccharide, a carbohydrate, a lipid and a complex thereof.